Virginia Department of Health
Viral Hemorrhagic Fever (VHF): Guidance for Healthcare Providers
Key Medical and Public Health Interventions After Identification of a Suspected Case

1. Clinical Manifestations

A. Filoviruses (Ebola and Marburg)
Incubation period: Ebola- 2 to 21 days; Marburg- 2-14 days
Symptoms:
Ebola- High fever and severe prostration; diffuse maculopapular rash, which may occur by day 5 of illness; bleeding and disseminated intravascular coagulation (DIC).
Marburg- High fever; myalgias; nonpruritic maculopapular rash of the face, neck, trunk and arms; bleeding and DIC.

B. Arenaviruses (Lassa and New World hemorrhagic fever)
Incubation period: Lassa- 5 to 16 days; New World hemorrhagic fever- 7 to 14 days
Symptoms:
Lassa- Gradual onset of fever; nausea; abdominal pain; severe sore throat; conjunctivitis; ulceration of buccal mucosa; exudative pharyngitis; cervical lymphodenopathy. Late signs include severe swelling of head and neck; pleural and pericardial effusions. Hemorrhagic complications are less common.
New World hemorrhagic fever- Gradual onset of fever; myalgias; nausea; flushing of face and trunk; generalized lymphadenopathy. May develop petechiae, bleeding and central nervous system dysfunction.

C. Bunyaviruses[1] (Rift Valley fever)
Incubation period: 2 to 6 days
Symptoms: Fever; headache; retro-orbital pain; photophobia; jaundice. Less than 1% develop bleeding, DIC or encephalitis. Retinitis affects approximately 10% of patients, which may occur at time of acute febrile illness or up to 4 weeks later.

D. Flaviviruses[1] (Yellow fever; Omsk hemorrhagic fever; Kyanasur Forest disease)
Incubation period: Yellow fever- 3 to 6 days; Omsk and Kyasanur- 2 to 9 days
Symptoms:
Yellow fever- Fever; myalgias; facial flushing; conjunctival injection. Patients recover or enter a short remission, followed by fever, relative bradycardia, jaundice, renal failure, hemorrhagic complications.
Omsk hemorrhagic fever- Fever; conjunctivitis; papulovesicular eruption on soft palate; marked hyperemia of the face/trunk; generalized lymphadenopathy and splenomegaly. Patients may develop pneumonia and nervous system dysfunction.
Kyasanur Forest disease- Similar to Omsk hemorrhagic fever but biphasic illness: first phase lasts 6-11 days and is followed by an afebrile period of 9-21 days. Up to 50% of patients relapse and develop meningoencephalitis.

[1] Other hemorrhagic fever viruses exist in these categories; however, the viruses listed pose the most serious risk as biological weapons.

2. Identification of Suspected Cases

Early suspicion of VHF and immediate institution of VHF-specific isolation precautions can reduce the magnitude of outbreaks. Identify a suspected index case using the following clinical criteria: temperature ≥101ºF (38.3ºC) for less than 3 weeks duration; severe illness; at least 2 of the following hemorrhagic findings: hemorrhagic or purpuric rash, epistaxis, hematemesis, hemoptysis, blood in stool, or other hemorrhagic signs/symptoms; and no predisposing factors for hemorrhagic manifestations.[2]

Report suspected cases immediately to infection control, lab personnel (before any specimens are submitted for routine testing), and public health.

3. VHF-Specific Infection Control Precautions

The following precautions must be strictly followed for filoviruses, arenaviruses and suspected VHF of unknown type:

- Strict adherence to hand hygiene: *Wash hands prior to donning personal protective equipment for patient contact. After patient contact, remove gown, leg/shoe coverings, and gloves, and immediately clean hands. It is important to wash hands prior to the removal of respirators, face shields, and goggles to minimize exposure of mucous membranes. Wash hands once again after the removal of respirators, face shields and goggles.*
- Double gloves
- Impermeable gowns
- N-95 masks or better
- Negative pressure isolation room with 6-12 air changes per hour, air exhausted directly to the outdoors or passage through a high-efficiency particulate air (HEPA) filter before recirculation, and door kept closed.[3]
- Leg and shoe coverings
- Face shields
- Goggles for eye protection
- Restricted access of nonessential staff and visitors to patient's room
- Dedicated medical equipment, such as stethoscopes, glucose monitors, and, if available, point-of-care analyzers
- Concurrent disinfection: Patient's excreta, sputum, blood, all objects with which the patient has had contact, and laboratory equipment should be disinfected with a solution of 1 part household bleach to 9 parts water (0.5% sodium hypochlorite solution) or a 0.5% phenol solution with detergent.
- If multiple patients with viral hemorrhagic fever are in a health care facility, they should be cared for in the same part of the hospital to minimize exposures to others.
- Contaminated protective coverings should immediately be double-bagged and washed (without sorting) in hot water with bleach or, alternatively, autoclaved or incinerated.
- See *Part 8, Decontamination*, for additional hospital room recommendations.

For bunyaviruses and flaviviruses, use standard and contact precautions.

[2] Criteria are adapted from the World Health Organization's surveillance standards for acute hemorrhagic fever syndrome.
[3] Resources may not be possible in many facilities or in a situation where many persons are ill with suspected VHF. For such situations, all other measures should be taken and would, in combination, be expected to diminish the risk of nosocomial spread.

4. Handling Laboratory Specimens

Hemorrhagic fever viruses are highly infectious in the laboratory setting and may be transmitted to laboratory personnel via small-particle aerosols or via contact with infectious specimens or equipment contaminated by infectious specimens. Laboratory staff must be alerted to any suspected diagnosis of VHFs and reminded of the risk of transmission in the laboratory setting. No specimens should be sent to any laboratory until infection control plans have been instituted for transport of specimens, containment during laboratory testing, and disinfection of equipment.

Laboratory tests should be limited to only critical diagnostic tests. If possible, these should be performed at bedside using dedicated point-of-care analyzers. However, if specimens must be sent to the clinical laboratory, maximum precautions must be exercised, as described below:

Specimen transport: Specimens for laboratory testing should be clearly identified, double bagged, and hand carried to the laboratory (never via pneumatic tube). Laboratory and infection control personnel must be notified before specimens are sent. Specimens should be received and handled only by specially designated individuals.

Routine laboratory testing: Specimens should be tested only by dedicated, trained laboratory personnel wearing personal protective equipment that ensures barrier and airborne precautions. If possible, all laboratory tests should be carried out in special high containment facilities. If not, the minimum containment should be handling of all specimens within a class 2 Biological Safety Cabinet using BSL-3 practices, including airborne precautions. Methods for decreasing infectivity of serum before routine testing have been described.[4] [5] Infectious specimens from VHF patients, including blood and urine, must be autoclaved or incinerated before disposal.

Decontamination of laboratory equipment: Any laboratory equipment contaminated with infectious patient specimens should be disinfected with 0.5% sodium hypochorite solution (1:10 dilution of household bleach made up fresh daily) or 0.5% phenol with detergent, and, as far as possible, appropriate heating methods such as autoclaving, incineration, or boiling should be used.[5]

Laboratory testing for VHF agents: Specific testing for VHF agents is available at the Centers for Disease Control and Prevention (CDC), and is performed under BSL-4 containment. Diagnostic tests include IgM antibody detection by antigen-capture ELISA, RT-PCR, and viral isolation. Testing must be arranged by consultation with the health department or the Division of Consolidated Laboratory Services (DCLS). (See the VDH document entitled "*Guidance for Submitting Specimens for Laboratory Diagnosis of Viral Hemorrhagic Fever*"). Contact DCLS via emergency pager at 804-418-9923 (24hr/7days) for consultation on shipping and packaging biological agents to CDC. Package in accordance with International Air Transport Association (IATA) regulations to prevent leakage. The Office of Health and Safety, Biosafety Branch (OHS) at CDC provides guidance on the packaging and shipping of biomedical material. See:

(IATA: **http://www.iata.org/cargo/dg/iata.htm)**
(OHS: **http://www.cdc.gov/od/ohs/biosfty/shipdir.htm)**

[4] Borio L; Inglesby T; Peters CJ et al. Hemorrhagic Fever Viruses as Biological Weapons: Medical and Public Health Management. *JAMA.* 287 (18): 2391-2405, 2002.
[5] Chin, J. ed., Control of Communicable Diseases Manual, Seventeenth Edition, American Public Health Association, Washington, DC, 2000.

5. Diagnosis

For naturally occurring infections, patients are likely to have traveled to Africa or Asia and handled animal carcasses, had contact with sick animals or people, or had arthropod bites within twenty-one days of onset of symptoms. A high index of suspicion will be required to diagnose VHF among persons exposed to a covert bioterrorist attack.

Prompt reporting to public health authorities should occur for any patient with: acute onset of fever of less than three weeks duration; severe illness; any two of the following: hemorrhagic or purpuric rash, epistaxis, hematemesis, hemoptysis, blood in stool, or other hemorrhagic signs/symptoms; and no known predisposing factors for hemorrhagic manifestations.

6. Treatment

Initiate supportive and ribavirin therapy (See Table 1), while diagnostic confirmation is pending. If infection with arenavirus or bunyavirus is confirmed, continue ten day course of ribavirin. Discontinue ribavirin if an infection with filovirus or flavivirus is confirmed, or if the diagnosis of VHF is excluded or an alternate diagnosis is established.

Table 1. Ribavirin Therapy

Contained Casualty Setting	Severe Circumstances Setting: *Regimens may be used for treatment in severe circumstances when IV treatment is impractical or unavailable.*
Adults (including pregnant women)	
Loading dose of 30 mg/kg IV (maximum 2 g) once, followed by 16 mg/kg IV (maximum 1g/dose) every 6 hours for 4 days, followed by 8mg/kg IV (maximum 500 mg/dose) every 8 hours for 6 days.	Loading dose of 2000 mg orally once, followed by 1200 mg/d orally in 2 divided doses (if weight > 75 kg) or 1000 mg/d orally in 2 doses (400 mg in AM and 600 mg in PM) for 10 days.
Children	
Same as for adults, dosed according to weight.	Loading dose of 30 mg/kg orally once, followed by 15 mg/kg per day orally in 2 divided doses for 10 days.

The US Food and Drug Administration has not approved treatment regimens shown in the chart.

7. Post-Exposure Surveillance

Laboratory workers processing specimens, all known high risk and close contacts of individuals with a filovirus or arenavirus, and other persons considered potentially exposed should be placed under medical surveillance for 21 days after potential exposure.[6] Individuals should record their temperatures twice daily and report any temperature of $\geq$101°F to public health authorities. If a temperature $\geq$101°F is reported, ribavirin therapy should be initiated unless an alternative diagnosis is established or agent is known to be a filovirus or flavivirus.

[6] High-risk contacts are individuals who have had mucous membrane contact with a patient (e.g. kissing or sexual intercourse) or have had percutaneous contact with a patient's secretions, excretions or blood. Close contacts are those who live with, shake hands with, hug, process laboratory specimens from, or care for a patient with clinical evidence of a viral hemorrhagic fever, prior to initiation of appropriate precautions.

8. Decontamination

Linen handlers and workers involved in environmental decontamination should wear personal protective equipment outlined under *Part 3,VHF-Specific Infection Control Precautions*. Contaminated linens should be doubled-bagged and washed without sorting in a hot water cycle with bleach or alternatively, autoclaved or incinerated. Surfaces in patient rooms and contaminated medical equipment should be disinfected with a solution of 1 part household bleach to 9 parts water (0.5% sodium hypochlorite solution) or a 0.5% phenol solution with detergent.

9. Postmortem Practices

Contact with cadavers has been implicated as a source of transmission in previous outbreaks. Prompt burial or cremation of the deceased, with minimal handling, is recommended. No embalming should be done. If autopsies are done, they should be performed by specially trained persons using VHF-specific barrier precautions, HEPA-filtered respirators and negative-pressure rooms.

10. Public Health Measures

A. Suspected cases should be reported immediately to hospital epidemiology/infection control, who in turn should immediately notify laboratory personnel, other medical care providers and the local public health department.
B. Arrange for laboratory testing for agents of VHF by consulting with the local health department or the Division of Consolidated Laboratory Services (DCLS) at 804-418-9923 (24 hour/7 day). DCLS will coordinate the submission of specimens to CDC.
C. Designated public health authorities should immediately begin an epidemiologic investigation, including identification of close and high-risk contacts (who should be placed under medical surveillance for 21 days from day of suspected/known exposure) and identification of a possible index case. Patients should be advised to refrain from unprotected sexual activity for three months after clinical recovery, since virus has been isolated in seminal fluid for up to three months.

Information excerpted from: Borio L; Inglesby T; Peters CJ et al. Hemorrhagic Fever Viruses as Biological Weapons: Medical and Public Health Management. *JAMA*. 2002; 287 (18):2391-2405.

Clinical Terms Related to Viral Hemorrhagic Fever

Conjunctival injection:	Red/bloodshot eyes
Disseminated intravascular coagulation (DIC):	Disorder that occurs when blood clotting mechanisms are activated throughout the body instead of being localized to an area of injury.
Epistaxis:	Bleeding from the nose
Hematemesis:	Vomiting of blood
Hemoptysis:	Spitting of blood derived from the lung or bronchial tubes as a result of pulmonary or bronchial hemorrhage
Hyperemia:	Presence of an increased amount of blood flow in a part or organ